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Biocompatibility Assessments of Surgical sutures: The Guinea Pig Maximization Test

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Abstract : Surgical suture is a medical device used to hold body tissues together after an injury or surgery. Application generally involves using a needle with an attached length of thread as evaluated for the potential to cause delayed skin contact sensitization in a Closed-patch test**.** This study was conducted base on the requirements of ISO 10993-10: Biological Evaluation of Medical Devices-Part 10: Tests for Irritation and Skin Sensitization. The guinea pig maximization test (GPMT) is made of the potential of the material under test to produce skin sensitization. The polar and nonpolar extracts were prepared by using saline solution and olive oil, respectively, after sinking the materials tested (2.0 g) in 10 ml of the corresponding liquid. Incubation was carried out at the temperature of 37 °C for 72 h. The saline solution and pure olive oil were used as negative control samples and were incubated under the same conditions as above. The guinea pig maximization test (GPMT) consist of intradermal induction phase, topical induction patches and challenge phase. Following a intradermal induction phase, The test item extract with polar and non polar solvent were injected in clipping area of each animal in test group and control group, respectively. Following a challenge phase, the test group and control group were challenged with the test item. No evidence of sensitization was observed. Individual results of skin scoring for the induction phase and the challenge phase is 0.0.
Keyword : Surgical suture,Intravenous reactivity test.

Introduction

Polymeric materials have dramatically influenced our day to day life. They find potential in various fields like food packaging, automobiles, water purification etc.[1-3] Application of polymeric biomaterials in medicine has been a thrust area of research owing to the exceptional and superior properties they exhibit.[4] The increased use of polymeric biomaterials in the form of surgical implants, sutures and scaffolds for biomedical applications.[5]

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Surgical suture is a medical device used to hold body tissues together after an injury or surgery. Application generally involves using a needle with an attached length of thread. A number of different shapes, sizes, and thread materials have been developed over its millennia of history. Surgeons, physicians, dentists, podiatrists, eye doctors, registered nurses and other trained nursing personnel, medics, and clinical pharmacists typically engage in suturing. Surgical knots are used to secure the sutures.[6]

The primary purpose of suture is to hold apposing tissues together to facilitate and hasten healing process with minimal or no scar formation following an injury or surgical procedure.[7] A variety of materials such as gold, silver, iron and steel wires, dried animal gut, animal hair (e.g. horse hair), silk, tree bark and plant fiber (e.g. linen, cotton) were used as suture materials in the past, while some of them are still use. The recent has witnessed the use of various synthetic biomaterials such as polydioxanone, poly(lactic-co-glycolic acid) as suture materials.[8]

To minimize any potential hazards to the patients, it is essential that biocompatibility assessments be conducted for surgical suture made from Polyglycolide-Co-L-Lactide that are used in medical devices. The common tests are used to measure biocompatibility: ISO10993-10, Biological Evaluation of Medical Devices (2010).[9]

Animals and Husbandry

The albino Dunkin Hartley guinea pig has been used for sensitization studies. Repeated patching of the test item to fur clipped intact skin will be employed. Topical applications are related to the human exposure route and permit the evaluation of dermal contact and/or absorption of potential sensitization. Reactions directly under the topical application site can be observed.

Animals and husbandry were conducted based on the test guidance of The International Organization for Standardization 10993-2, Biological Evaluation of Medical Devices-Part 2: Animal Welfare Requirement, 2006[10], The International Organization for Standardization 10993-10, Biological evaluation of medical devices Part 10 Test for irritation and delayed type hypersensitivity, 2010[9] and Guidelines of "Guide for the care and use of laboratory animals" (Institute of laboratory animal resources, National academic press 2011; NIH publication number #85-23, revised 2011).

The healthy young guinea pig of body weight in range 300 - 500 g were obtained from Office of Laboratory Animal Production, NLAC, Mahidol University, Thailand. The animals were kept under standard conditions 12:12 (light : dark cycles) at 22±3 0C and 30-70% relative humidity. The animals were housed individually in cages. The animals were fed with feed and chlorinated water *ad libitum*. All the animals were acclimatized for 5 days prior to the study. The study was approved by National Laboratory Animal Center Animal Care and Use Committee (NLAC-ACUC), Mahidol University; Thailand.

Preparation of the test material extracts

The surgical suture (Polyglycolide-Co-L-Lactide) and control item preparation was conducted based on the test guidance of the International Organization for Standardization 10993-12, Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials, 2007.[11]

Polar solvent (Physiological saline) and Non polar solvent (olive oil) were used as a control item.

Two grams of the surgical suture (Polyglycolide-Co-L-Lactide) was extracted in Polar solvent and Non polar solvent. The solutions were performed in a water bath at 37ºC for 72 hours. Polar solvent and non polar solvent which had no contact with the surgical suture were use as negative control and were incubated under the same conditions as above. The extracts were used within 4 hours to perform the test procedure. [11]

Intradermal Induction phase

Fur on the back of each animal was clipped with an electric clipper 16 – 24 hours prior to exposure. On the day of exposure, the clipped area was separated to 2 sites on each animal. The surgical suture (Polyglycolide-Co-L-Lactide) extraction and control item were intracutaneous (Intradermal) applied to the test sites and control sites respectively.

The animals in test group and control group were injected with 0.1 ml intradermal in the clipped area. The injection sites (A, B and C) as Site A: A 50:50 volume ratio stable emulsion of Freund's complete adjuvant mixed with the solvent and use 0.9% sodium chloride for water soluble material. Site B: The test animals were injected with test item extraction and control animals were injected with the solvent alone. Site C: The test animals were injected with test item extraction diluted in 50:50 volume ratio stable emulsion of Freund's complete adjuvant and the solvent. The control animals were injected with an emulsion of blank liquid with adjuvant.

Topical Induction phase

At 7 days after completion of intradermal induction phase, the fur of all test and control group were clipped with an electric clipper. All test and control animals were administrated the test item by topical application to the intrascapular region of each animals, using a patch approximately. The 10% sodium dodecyl sulfate was massaged in to skin 24+2 hours before the topical induction. The concentration for site B was selected to applied to the intrascapular region. The patchs were removed after 48+1 hours.

Challenge phase

At 14 days after the topical induction application, the fur of all test and control group were clipped with an electric clipper. All test and control animals were topical exposure with the concentration for site C (except Freund's complete adjuvant) of test item and blank to sites that were not treated during the induction phase such as the upper flank of each animals. The soaked chambers were used for application and secure with an occlusive dressing. The occlusive dressings were removed after 24+1 hours.

Observation

All animals (test groups and control groups) were observed daily for general health. The body weights were recorded weekly.

The observations for skin reactions were conducted at 24 hours and 48 hours after occlusive dressing removals. The scores were recorded in accordance with the criteria present below Table 8. Magnusson and kligman scale.

Evaluation of result

The response from the induction phase and challenge phase were compared within the test group and control group. The test item is graded according to the criteria present below Magnusson and kligman scale**.**

Table 1. Magnusson and Kligman scale

Patch test reaction	Grading score
No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Intense erythema and/or swelling	3

Result

At the first day, The clinical observations and individual body weights of test group control group were clinically normal. After intradermal induction, all animals gained weight during the course of the study.

Under the condition of intradermal induction phase, At the skin injection sites with Freund's complete adjuvant, increased swelling and hemorrhagic reaction followed by a definite necrotic reaction occurred. Severe corneal reactions were also observed in the animals.

Under the condition of this study, the surgical suture (Polyglycolide-Co-L-Lactide)) and solvents (Physiological saline and olive oil) showed no evidence of causing delayed sensitization. Individual results of skin scoring of the test group and control group are 0.0 for the challenge phase. The individual score for Induction phase and challenge phase are presented.

Conclusion and Discussion

Biocompatibility is a general term used to describe the suitability of a material for exposure to the body or bodily fluids. Biocompatibility testing is essential for all materials that will be used in medical devices to minimize any potential hazards to the patient. A material will be considered biocompatible if it allows the body to function without any complications, such as allergic reactions, irritation or other adverse side effects. The present study can by considered as a part of the whole biocompatibility testing.

Surgical sutures as a medical device in wound management and recent advancements have expanded its applicability and efficacy. Major progress in this front can be attributed toward the technological advancements in materials science. Polymers hold a significant potential with their high flexibility giving rise to diverse suture materials with excellent physical and mechanical properties. In addition, to better handling qualities and desired modifications, it should also be non carcinogenic, nontoxic, free of allergens, and importantly it should not evoke any adverse response in the host tissues. To meet these requirements, it is necessary to conduct detailed pre-clinical studies and evaluate the safety and efficacy in human trials on these emerging sutures. The next generation of suture materials, an outcome of multidisciplinary efforts has immense potential to impact surgical outcomes and wound management.

Table 2. Skin Scoring effects of intracutaneous (i.c.) administration of Physiological saline extract (0.1 ml) of surgical suture (Polyglycolide-Co-L-Lactide).

Group	No.	Skin Reaction			Skin Scoring Index
		24h	48h	72h	
surgical suture (Polyglycolide-Co-L-Lactide) extract with Physiological saline	1	0	0	0	0.0
	2	0	0	0	0.0
	3	0	0	0	0.0
	4	0	0	0	0.0
	5	0	0	0	0.0
	6	0	0	0	0.0
	7	0	0	0	0.0
	8	0	0	0	0.0
	9	0	0	0	0.0
	10	0	0	0	0.0

Table 3. Skin Scoring effects of intracutaneous (i.c.) administration of Physiological saline extract (0.1 ml).

Group	No.	Skin Reaction			Skin Scoring Index
		24h	48h	72h	
Physiological saline	1	0	0	0	0.0
	2	0	0	0	0.0
	3	0	0	0	0.0
	4	0	0	0	0.0
	5	0	0	0	0.0
	6	0	0	0	0.0
	7	0	0	0	0.0
	8	0	0	0	0.0
	9	0	0	0	0.0
	10	0	0	0	0.0

Table 4. Skin Scoring effects of intracutaneous (i.c.) administration of Olive oil extract (0.1 ml) of surgical suture (Polyglycolide-Co-L-Lactide).

Group	No.	Skin Reaction			Skin Scoring Index
		24h	48h	72h	
surgical suture (Polyglycolide-Co-L-Lactide) extract with olive oil	1	0	0	0	0.0
	2	0	0	0	0.0
	3	0	0	0	0.0
	4	0	0	0	0.0
	5	0	0	0	0.0
	6	0	0	0	0.0
	7	0	0	0	0.0
	8	0	0	0	0.0
	9	0	0	0	0.0
	10	0	0	0	0.0

Table 5. Skin Scoring effects of intracutaneous (i.c.) administration of Olive oil extract (0.1 ml).

Group	No.	Skin Reaction			Skin Scoring Index
		24h	48h	72h	
olive oil	1	0	0	0	0.0
	2	0	0	0	0.0
	3	0	0	0	0.0
	4	0	0	0	0.0
	5	0	0	0	0.0
	6	0	0	0	0.0
	7	0	0	0	0.0
	8	0	0	0	0.0
	9	0	0	0	0.0
	10	0	0	0	0.0

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